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Case of Indolent Endocarditis Due to *Pseudomonas stutzeri* with Genetic Evidence of Relapse after 4 Years▽

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***Pseudomonas stutzeri*, a gram-negative bacterium, is a common inhabitant of soil and water. We report an unusual case of a relapse of infective endocarditis due to *P. stutzeri* 4 years after the initial episode. The identity of the strains was proven by genomic analysis.**

CASE REPORT

A 40-year-old woman was admitted to our hospital for persistent fever in 2007. She had undergone aortic valve replacement and mitral valvuloplasty in 1991 for a valvulopathy of rheumatic origin, followed by mitral and aortic replacements with mechanical prostheses in 1996 and 1997, respectively, for histologically proven infective endocarditis (IE) without microbiological documentation. In November 2001 and July 2002, transesophageal echography (TEE) was performed for fever but did not show any abscess around the prosthetic aortic valve. In December 2003, after 3 weeks of fever treated by antibiotics (unknown regimen), she was admitted for a second-degree auriculo-ventricular block, revealing at TEE a healed abscess of the aortic ring. One out of four sets of blood cultures yielded colonies, which adhered to agar, of a growth-deficient aerobic gram-negative bacillus (no certain identification was obtained) that was susceptible to cefotaxime (MIC, 2 mg/liter in Mueller-Hinton agar supplemented with 5% horse blood), ciprofloxacin, gentamicin, and tetracycline but resistant to amoxicillin and amoxicillin-clavulanic acid. Because of the suspicion of EI in the absence of other foci of infection, the patient was treated with cefotaxime for 1 month, followed by ceftriaxone for another month. Blood cultures remained negative, and the patient remained without fever. A few months later, histologically proven pulmonary sarcoidosis without cardiac involvement was diagnosed and the patient was given prednisolone at 1 mg/kg/day.

In 2007, a physical examination yielded no signs of IE. Sarcoidosis was quiescent under prednisolone treatment at 6 mg/day. The white blood cell count was 14.2×10^9 cells/liter (90% polymorphonuclear), and the C-reactive protein (CRP) level was 35.6 mg/liter (N, <10 mg/liter). Two out of three aerobic blood cultures, started at a 24-h interval in the absence of antibiotic treatment, were positive after 4 days, yielding a gram-negative bacillus with the same cultural characteristics, i.e., improvement of bacterial growth in medium supplemented with horse blood and the same antibiotic susceptibility and resistance profile as described above. TEE revealed a newly apparent moderate aortic regurgitation. The initial treatment was cefotaxime and gentamicin for 14 days. After 4 days, the patient became afebrile and her white blood cell count and CRP level dropped to 10.1×10^9 cells/liter and 12 mg/liter, respectively. A thoracoabdominal computed tomography scan and vertebral column magnetic resonance imaging were normal. 16S rRNA gene amplification and sequencing led to the identification of *Pseudomonas stutzeri*. Antibiotic therapy was changed to oral ciprofloxacin and doxycycline since the patient refused prolonged intravenous therapy. Cardiac surgery was not performed because of the high risk of death. After 16 months of treatment, the patient is in stable cardiac condition and the CRP level is below 15 mg/liter. The serum trough concentrations of ciprofloxacin and doxycycline were 1.1 and 2.4 mg/liter, respectively. Repeated blood cultures have been negative.

The isolate from 2003 was recovered and identified as *P. stutzeri* by the method described above. Analysis of the genomic fingerprints of both isolates, after random amplification by PCR (6), showed that they were highly related (Fig. 1).

Human cases of *P. stutzeri* infection are rare and concern mostly immunocompromised patients with underlying diseases or previous surgery (2). By the modified Duke criteria of endocarditis (3), the patient was classified as having definite IE (she met two major criteria in 2007 and one major and three minor criteria in 2003). To our knowledge, this is the second reported case of IE due to *P. stutzeri*. The first was that of a 68-year-old man with IE with a bioprosthesis who was successfully treated with tobramycin and mezlocillin (5). As in the present report, the portal of entry and the source of infection were not identified. Peroperative contamination during the

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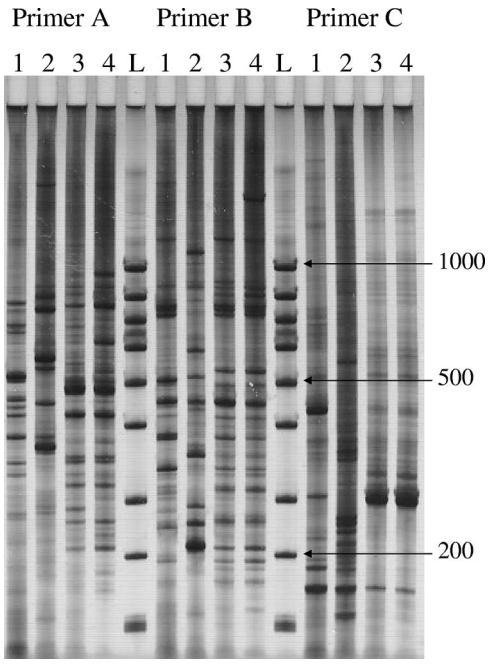

FIG. 1. DNA fragment banding pattern as visualized after acrylamide gel electrophoresis of PCR products obtained by random amplification of polymorphic DNA with three primers (A, B, and C [6]) and silver staining. Lanes: 1 and 2, control clinical strains of *P. stutzeri*; 3, *P. stutzeri* isolated in 2007; 4, *P. stutzeri* isolated in 2003; L, DNA ladder (the molecular sizes on the right are in base pairs).

surgery performed in 1997 is possible, but the interval (6 years) between the last surgery and the first episode of *P. stutzeri* bacteremia does not support this hypothesis.

Recurrent IE due to the same microorganism is rare (ca. 3% of IE cases; 1, 4) and can be caused by relapse or reinfection, usually distinguished by a delay of recurrence of less or more than 6 months, respectively (4). However, a relapse after 9 months has been described (1). We report here a unique delay of 4 years for relapsing endocarditis proven by genomic strain analysis. Reinfection with the same *P. stutzeri* strain would have been highly improbable considering the genetic variability of this species (6) and in the absence of plausible exposure given the patient's lifestyle. We hypothesize that the moderate activity of cefotaxime against members of the family *Pseudomonadaceae*, reflected by the clinical improvement in 2003, possibly in conjunction with the particularly low virulence of the strain living in a dormant state, may explain the delayed relapse despite the presence of the mechanical valve. A prolonged follow-up is necessary to ensure the definite cure of this EI.

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